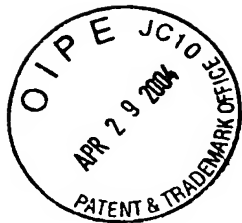


04-30-04



EXPRESS MAIL NO. EV 335 859 756 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Friedman *et al.*

Confirmation No.: 5401

Application No.: 10/685,722

Group Art Unit: 1614

Filed: October 14, 2003

Examiner: To be assigned

For: BENZOPYRANONE COMPOUNDS, COMPOSITIONS THEREOF, AND METHODS FOR TREATING AND PREVENTING CANCER
Attorney Docket No.: 10624-111-999

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §§ 1.56 and 1.97

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure imposed by 37 C.F.R. §§ 1.56 and 1.97 to inform the Patent and Trademark Office of all references coming to the attention of each individual associated with the filing and prosecution of the above-identified application that are or may be related to patentability of the claimed invention, Attorneys for Applicants hereby invite the Examiner's attention to references **A01-A5, B01-B02 and C01-C89** which are listed on the accompanying Form PTO-1449 entitled "List of References Cited By Applicant."

Copies of references **A01-A5, B01-B02 and C01-C89** are submitted herewith. Identification of the listed references is not to be construed as an admission that such references are available as "prior art" against the subject application.

Applicants request that the Examiner review all the references identified on the attached Form PTO-1449, and that they be made of record in the file history of the above-identified application.

As this Information Disclosure Statement is being filed before the mailing date of the first Office Action on the merits, Applicants estimate that no fee is required. Should a fee be required, please charge the required fee to Jones Day Deposit Account No. 503013. A duplicate of this sheet is enclosed for accounting purposes.

Respectfully submitted,

Anthony M. Insogna, Reg. No. 35,203

By: *Michael D. Byrnes, Reg. No. 47,458* 35,203

Date April 29, 2004

Anthony M. Insogna

(Reg. No.)

JONES DAY

222 East 41st Street

New York, New York 10017

(212) 326-3939

LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary)	ATTY DOCKET NO.	APPLICATION NO
	10624-111-999	10/685,722
	APPLICANT	CONFIRMATION NO
	Friedman et al.	5401
	FILING DATE	GROUP
	October 14, 2003	1614



U.S. PATENT DOCUMENTS

*EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A01	2003/0149025	8/7/03	Zeldis		
	A02	6,620,838	9/16/03	McKie et al.		
	A03	6,372,739	4/16/02	Stein et al.		
	A04	6,331,562	12/18/01	Bhagwat et al.		
	A05	6,291,456	9/18/01	Stein et al.		

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
						YES NO
	B01	WO 01/49673	7/12/01	PCT		
	B02	WO 00/39120	7/6/00	PCT		

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

C01	Al-Saffar et al., 1996, "Assessment of the role of GM-CSF in the cellular transformation and the development of erosive lesions around orthopaedic implants", Am J Clin Pathol. 105(5):628-39.
C02	Alonzi et al., 1998, "Interleukin 6 is required for the development of collagen-induced arthritis", J Exp Med. 187(4):461-8.
C03	Barkhem et al., 1998, "Differential response of estrogen receptor alpha and estrogen receptor beta to partial estrogen agonists/antagonists", Mol Pharmacol. 54(1):105-12.
C04	Bismar et al., 1995, "Increased cytokine secretion by human bone marrow cells after menopause or discontinuation of estrogen replacement", J Clin Endocrinol Metab. 80(11):3351-5.
C05	Bodine et al., 1998, "Estrogen receptor-alpha is developmentally regulated during osteoblast differentiation and contributes to selective responsiveness of gene expression", Endocrinology. 139(4):2048-57.
C06	Brandenberger et al., 1998, "Estrogen receptor alpha (ER-alpha) and beta (ER-beta) mRNAs in normal ovary, ovarian serous cystadenocarcinoma and ovarian cancer cell lines: down-regulation of ER-beta in neoplastic tissues", J Clin Endocrinol Metab. 83(3):1025-8.
C07	Chen et al., 2001, "Molecular basis for the constitutive activity of estrogen-related receptor alpha-1", J Biol Chem. 276(30):28465-70.
C08	Chung et al., 2002, "Resistance to tamoxifen-induced apoptosis is associated with direct interaction between Her2/neu and cell membrane estrogen receptor in breast cancer", Int J Cancer. 97(3):306-12.
C09	Clinton and Hua, 1997, "Estrogen action in human ovarian cancer", Crit Rev Oncol Hematol. 25(1):1-9.
C10	Cooke et al., 1998, "Mechanism of estrogen action: lessons from the estrogen receptor-alpha knockout mouse", Biol Reprod. 59(3):470-5.
C11	Couse et al., 1997, "Tissue distribution and quantitative analysis of estrogen receptor-alpha (ERalpha) and estrogen receptor-beta (ERbeta) messenger ribonucleic acid in the wild-type and ERalpha-knockout mouse", Endocrinology. 138(11):4613-21.
C12	Coward et al., 2001, "4-Hydroxytamoxifen binds to and deactivates the estrogen-related receptor gamma", Proc Natl Acad Sci U S A. 98(15):8880-4.
C13	Das et al., 1997, "Estrogenic responses in estrogen receptor-α deficient mice reveal a distinct estrogen signaling pathway", Proc. Natl. Acad. Sci. USA 94:12786-91
C14	Devlin et al., 1998, "IL-6 mediates the effects of IL-1 or TNF, but not PTHrP or 1,25(OH)2D3, on osteoclast-like cell formation in normal human bone marrow cultures", J Bone Miner Res. 1998 Mar;13(3):393-9.
C15	Duan et al., 1998, "Estrogen-induced c-fos protooncogene expression in MCF-7 human breast cancer cells: role of estrogen receptor Sp1 complex formation", Endocrinology. 139(4):1981-90.

C16	Enmark et al., 1997, "Human estrogen receptor beta-gene structure, chromosomal localization, and expression pattern", J Clin Endocrinol Metab. 82(12):4258-65.
C17	Eustace et al., 1993, " Interleukin-6 (IL-6) functions as an autocrine growth factor in cervical carcinomas in vitro", Gynecol Oncol. 50(1):15-19.
C18	Farhat et al., 1996, "The vascular protective effects of estrogen", FASEB J. 10(5):615-24.
C19	Garrett et al., 1997, "A murine model of human myeloma bone disease", Bone 20(6):515-20.
C20	Girasole et al., 1992, "17 beta-estradiol inhibits interleukin-6 production by bone marrow-derived stromal cells and osteoblasts in vitro: a potential mechanism for the antiosteoporotic effect of estrogens", J Clin Invest. 89(3):883-91.
C21	Grese et al., 1997, " Structure-activity relationships of selective estrogen receptor modulators: modifications to the 2-arylbenzothiophene core of raloxifene", J Med Chem. 40(2):146-67.
C22	Gupta et al., 1985, "7-hydroxy-4-phenyl-3(4-hydroxyphenyl)-coumarin--a new interceptive agent", Indian J Exp Biol. 23(1):638-40.
C23	Gustafsson et al., 1998, "Therapeutic potential of selective estrogen receptor modulators", Curr Opin Chem Biol. 2(4):508-11.
C24	Hata et al., 1998, "Role of estrogen and estrogen-related growth factor in the mechanism of hormone dependency of endometrial carcinoma cells", Oncology. 55 Suppl 1:35-44.
C25	Hughes et al., 1996, "Estrogen promotes apoptosis of murine osteoclasts mediated by TGF-beta", Nat Med. 2(10):1132-6.
C26	Iafrati et al., 1997, "Estrogen inhibits the vascular injury response in estrogen receptor alpha-deficient mice", Nat Med. 3(5):545-8.
C27	Jansson et al., 1994, " Estrogen induces a potent suppression of experimental autoimmune encephalomyelitis and collagen-induced arthritis in mice", J Neuroimmunol. 53(2):203-7.
C28	Jeltsch et al., 1987, "Structure of the human oestrogen-responsive gene pS2", Nucleic Acids Res. 15(4):1401-14.
C29	Jilka et al., 1995, "Estrogen loss upregulates hematopoiesis in the mouse: a mediating role of IL-6", Exp Hematol. 23(6):500-6.
C30	Jilka et al., 1992, "Increased osteoclast development after estrogen loss: mediation by interleukin-6", Science 257(5066):88-91.
C31	Kelly et al., 1999, "Estrogen Modulation of G-protein-coupled Receptors", Trends Endocrinol Metab. 10(9):369-374.
C32	Kimble et al., 1996, "Estrogen deficiency increases the ability of stromal cells to support murine osteoclastogenesis via an interleukin-1 and tumor necrosis factor-mediated stimulation of macrophage colony-stimulating factor production", J Biol Chem. 271(46):28890-7.
C33	Kimble et al., 1995, " Simultaneous block of interleukin-1 and tumor necrosis factor is required to completely prevent bone loss in the early postovariectomy period", Endocrinology. 136(7):3054-61.
C34	Klein et al., 1991, "Murine anti-interleukin-6 monoclonal antibody therapy for a patient with plasma cell leukemia", Blood. 78(5):1198-204.
C35	Klein et al., 1989, " Paracrine rather than autocrine regulation of myeloma-cell growth and differentiation by Interleukin-6", Blood. 73(2):517-26.
C36	Koo et al., 1992, " Interleukin-6 and renal cell cancer: production, regulation, and growth effects", Cancer Immunol Immunother. 35(2):97-105.
C37	Korach et al., 1994, "Insights from the study of animals lacking functional estrogen receptor", Science 266(5190):1524-7.
C38	Krege et al., 1998, "Generation and reproductive phenotypes of mice lacking estrogen receptor beta", Proc Natl Acad Sci U S A. 95(26):15677-82.
C39	Kuiper et al., 1997, " Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors alpha and beta", Endocrinology. 1997 Mar;138(3):863-70.
C40	Kurihara et al., 1989, " Generation of osteoclasts from isolated hematopoietic progenitor cells", Blood 74(4):1295-302.
C41	Laflamme et al., 1998, "Expression and neuropeptidergic characterization of estrogen receptors (ERalpha and ERbeta) throughout the rat brain: anatomical evidence of distinct roles of each subtype", J Neurobiol. 36(3):357-78.
C42	Lednicer et al., 1965, "Mammalian Antifertility Agents: Basic Ethers of 3,4 - Diphenylcoumarin", J. Med. Chem. 8:725-726
C43	Leisten, 1990 Interleukin-6 serum levels correlate with footpad swelling in adjuvant-induced arthritic Lewis rats treated with cyclosporin A or indomethacin. Clin Immunol Immunopathol. Jul;56(1):108-15.
C44	Levin et al., 1999, "Cellular Functions of the Plasma Membrane Estrogen Receptor", Trends Endocrinol Metab. 10(9):374-377.
C45	Lorenzo et al., 1987, "Colony-stimulating factors regulate the development of multinucleated osteoclasts from recently replicated cells in vitro", J Clin Invest. 80(1):160-4.
C46	Lu et al., 2001, " Transcriptional regulation of the estrogen-inducible pS2 breast cancer marker gene by the ERR family of orphan nuclear receptors", Cancer Res. 61(18):6755-61.
C47	MacDonald et al., 1986, "Effects of human recombinant CSF-GM and highly purified CSF-1 on the formation of multinucleated cells with osteoclast characteristics in long-term bone marrow cultures", J Bone Miner Res. 1(2):227-33.
C48	Martinez-Maza et al., 1992, "IL6 and AIDS", Res Immunol. 143(7):764-9.

	C49	Micheli et al., 1962, "Coumestrol, Plant Phenolics, and Synthetic Estrogens: a Correlation of Structure and Activity", 321-335
	C50	Nadal et al., 2001, "The plasma membrane estrogen receptor: nuclear or unclear?", Trends Pharmacol Sci. 22(12):597-9.
	C51	Ogawa et al., 1997, "Behavioral effects of estrogen receptor gene disruption in male mice", Proc Natl Acad Sci U S A. 94(4):1476-81
	C52	Ohshima et al., 1998, "Interleukin 6 plays a key role in the development of antigen-induced arthritis", Proc Natl Acad Sci U S A. 95(14):8222-6.
	C53	Okamoto et al., 1997, " Interleukin-6 as a paracrine and autocrine growth factor in human prostatic carcinoma cells in vitro", Cancer Res. 57(1):141-6.
	C54	Okamoto et al., 1997, "Autocrine effect of androgen on proliferation of an androgen responsive prostatic carcinoma cell line, LNCAP: role of interleukin-6", Endocrinology. 138(11):5071-4.
	C55	Pacifici 1996, "Estrogen, cytokines, and pathogenesis of postmenopausal osteoporosis", J Bone Miner Res. 11(8):1043-51.
	C56	Paech et al., 1997, " Differential ligand activation of estrogen receptors ERalpha and ERbeta at API sites", Science. 277(5331):1508-10.
	C57	Parfitt et al., 1996, " A new model for the regulation of bone resorption, with particular reference to the effects of bisphosphonates", J Bone Miner Res. 11(2):150-9.
	C58	Passeri et al., 1993, "Increased interleukin-6 production by murine bone marrow and bone cells after estrogen withdrawal", Endocrinology. 133(2):822-8.
	C59	Poli et al., 1994, "Interleukin-6 deficient mice are protected from bone loss caused by estrogen depletion", EMBO J. 13(5):1189-96.
	C60	Pollard et al., 1968, " The oestrogenic and anti-oestrogenic activity of some synthetic steroids and non-steroids", Steroids
	C61	Ray et al., 1987, "Enhanced antifertility activity of non-steroidal molecules with 3-n-butylamino-2-hydroxypropyloxy side chain", Contraception.35(3):283-7.
	C62	Reddy et al., 1994, " Interleukin-6 antisense deoxyoligonucleotides inhibit bone resorption by giant cells from human giant cell tumors of bone", J Bone Miner Res. 9(5):753-7.
	C63	Rissman et al., 1997, " Estrogen receptors are essential for female sexual receptivity", Endocrinology 138(1):507-10.
	C64	Rissman et al., 1997, " Estrogen receptor function as revealed by knockout studies: neuroendocrine and behavioral aspects", Horm Behav. 31(3):232-43.
	C65	Rohlf et al., 1998, "Prostate cancer cell growth inhibition by tamoxifen is associated with inhibition of protein kinase C and induction of p21(waf1/cip1)", Prostate. 37(1):51-9
	C66	Sar et al., 1999, "Differential expression of estrogen receptor-beta and estrogen receptor-alpha in the rat ovary", Endocrinology. 140(2):963-71.
	C67	Schiller et al., 1997, " 17Beta-estradiol antagonizes effects of 1alpha,25-dihydroxyvitamin D3 on interleukin-6 production and osteoclast-like cell formation in mouse bone marrow primary cultures", Endocrinology 138(11):4567-71.
	C68	Shinar et al., 1990, "The effect of hemopoietic growth factors on the generation of osteoclast-like cells in mouse bone marrow cultures", Endocrinology 126(3):1728-35.
	C69	Shughrue et al., 1997, "Responses in the brain of estrogen receptor alpha-disrupted mice", Proc Natl Acad Sci USA .94(20):11008-12.
	C70	Shughrue et al., 1997, "The distribution of estrogen receptor-beta mRNA in forebrain regions of the estrogen receptor-alpha knockout mouse", Endocrinology. 138(12):5649-52.
	C71	Shughrue et al., 1997, "Comparative distribution of estrogen receptor-alpha and -beta mRNA in the rat central nervous system", J Comp Neurol. 388(4):507-25.
	C72	Siegal et al., 1990, "Expression of the interleukin 6 receptor and interleukin 6 in prostate carcinoma cells", Cancer Res. 50(24):7786-8
	C73	Simpson et al., 1998, "Estrogen regulation of transforming growth factor-alpha in ovarian cancer", J Steroid Biochem Mol Biol. 64(3-4):137-45.
	C74	Stein et al., 1995, "Repression of the interleukin-6 promoter by estrogen receptor is mediated by NF-kappa B and C/EBP beta", Mol Cell Biol. 15(9):4971-9.
	C75	Suzuki et al., 1996, "Calcitonin-induced changes in the cytoskeleton are mediated by a signal pathway associated with protein kinase A in osteoclasts", Endocrinology. 137(11):4685-90.
	C76	Tartour et al., 1994, "Analysis of interleukin 6 gene expression in cervical neoplasia using a quantitative polymerase chain reaction assay: evidence for enhanced interleukin 6 gene expression in invasive carcinoma", Cancer Res. 54(23):6243-8.
	C77	Tremblay et al., 2001, " 4-Hydroxytamoxifen is an isoform-specific inhibitor of orphan estrogen-receptor-related (ERR) nuclear receptors beta and gamma. Endocrinology 142(10):4572-5.
	C78	Tremblay et al., 1998, "EM-800, a novel antiestrogen, acts as a pure antagonist of the transcriptional functions of estrogen receptors alpha and beta", Endocrinology 139(1):111-8.
	C79	Tsakamoto et al., 1992, "Interleukin-6 in renal cell carcinoma", J. Urol. 148(6):1778-81; discussion 1781-2.
	C80	Turner et al., 1998, "Differential responses of estrogen target tissues in rats including bone to clomiphene, enclomiphene, and zuclomiphene", Endocrinology. 139(9):3712-20.

C81	Verma et al., 1993, "Microwave induced alteration in the neuron specific enolase gene expression", Indian J. Chem. 32B:239-243.
C82	Weissglas et al., 1997, "The role of interleukin-6 in the induction of hypercalcemia in renal cell carcinoma transplanted into nude mice", Endocrinology 138(5):1879-85.
C83	Wendling et al., 1993, "Treatment of severe rheumatoid arthritis by anti-interleukin 6 monoclonal antibody", J Rheumatol. 20(2):259-62.
C84	Wyckoff et al., 2001, "Plasma membrane estrogen receptors are coupled to endothelial nitric-oxide synthase through Galpha(i)", J Biol Chem. 276(29):27071-6.
C85	Yamashita et al., 1998, "Endocrine therapy in pancreatic carcinoma", Oncology. 55 Suppl 1:17-22.
C86	Zhang et al., 1989, "Interleukin-6 is a potent myeloma-cell growth factor in patients with aggressive multiple myeloma", Blood. 74(1):11-3.
C87	Cohen et al., 1976, "Acute Nonlymphocytic Leukemia Associated with Nitrosourea Chemotherapy: Report of Two Cases", Cancer Treat Rep. 60:1257-61.
C88	Couldwell et al., 1996, "Treatment of Recurrent Malignant Gliomas with Chronic Oral High Dose Tamoxifen", Clin. Cancer Res. 2:619-622.
C89	Neubauer et al., 1995, "Raloxifene (LY156758) Produces Antimetastatic Responses and Extends Survival in the PAIII Rat Prostatic Adenocarcinoma Model", Prostate 27:220-9.

EXAMINER	DATE CONSIDERED
<p>*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	